

## MOMENTS

*The Problem of Moments.* By J. A. SHOHAT and J. D. TAMARKIN. xiv + 140 pp. American Mathematical Society.

THIS slim volume is the first in a series of "Mathematical Surveys," sponsored and published by the American Mathematical Society. And a good beginning it is. The authors have deftly assembled a wealth of results, mostly of somewhat specialized nature, and yet merging into general concepts.

The problem of moments, though rather special in its inception, was productive of the powerful concept of the Stieltjes integral and, in some measure, of the concept of an orthogonal system. In this respect, in the field of analysis it is second only to the problem of Fourier series which produced Cantor's set theory and Riemann's integral, and, to some extent, also Lebesgue's integral.

The authors are aware of this role of the moment problem but in outlining generalities they are brief and to the point. They succeed in introducing the

different variants of the moment problem as just so many problems in representing positive functionals on partially ordered function spaces, without mentioning the latter concept by name. Or again, they derive all pertinent facts about quasi-analytic functions as far as their problem is concerned without featuring the topic as such. However in expounding the connection with continued fractions they are emphatic in suggesting that, in substance, the problem is one of characterizing analytic functions of a complex variable whose imaginary part is positive in a half-plane. No account of such functions is complete without reference to Hermitian operators in Hilbert space, but the authors omit the reference for lack of space. The authors' heart is obviously in "classical" analysis, and so they include a chapter on approximate quadrature instead.

This and similar books will be a good reminder to younger mathematicians that "modern" mathematics is not all abstract spaces, group theory and such like.

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## SPECIAL ARTICLES

THE EFFECT OF pH ON THE AVAILABILITY OF *p*-AMINO BENZOIC ACID TO *NEUROSPORA CRASSA*<sup>1</sup>

SOME sulfonamides become more active as the pH is increased, this enhanced activity paralleling the ionization of the sulfonamide.<sup>2</sup> However, Schmelkes<sup>3</sup> has pointed out that sulfonamides which are so substituted as to preclude ionization also increase in activity as the pH is increased, a fact which is unexplained by the ionic theory of sulfonamide action. Since the undissociable sulfonamides supposedly do not undergo any change in the pH range involved, such an effect might be ascribed in part to decreased activity of *p*-aminobenzoic acid. The work of Brueckner<sup>4</sup> with *Staph. aureus* suggests that *p*-aminobenzoic acid, as well as the ionizable sulfonamides change in effectiveness as the pH is altered. But it is difficult to divorce the effect of pH on the sulfonamide from that on *p*-aminobenzoic acid in such bacterial inhibition experiments involving both of these compounds. The *Neurospora crassa* mutant of Tatum and Beadle was considered a more suitable test organism because it requires an exogenous supply of *p*-aminobenzoic acid, thus afford-

ing an opportunity to study the action of pH on the effectiveness of this substance alone.

The fungus was grown in a nutrient solution consisting of 25 g dextrose, 1 g potassium dihydrogen phosphate, 0.5 g magnesium sulfate, 2 g casein hydrolysate, 1.32 g Norit-purified fumaric acid, 0.2 ppm each of iron and zinc, 0.1 ppm manganese, 1 microgram biotin and 1,000 ml distilled water. Enough sodium hydroxide was added to adjust the pH to the various levels. Twenty-five ml of this solution was placed in 250 ml flasks, autoclaved, inoculated with a loopful of a suspension of germinating spores and incubated for 72 hours at 25° C. The mycelium was harvested, dried at 85° C. for 24 hours, and weighed.

TABLE 1

THE EFFECT OF pH ON THE GROWTH OF *Neurospora crassa* MUTANT IN THE PRESENCE OF VARIOUS AMOUNTS OF *p*-AMINO BENZOIC ACID

Micrograms of <i>p</i> -aminobenzoic acid per 25 ml of nutrient solution	The average weight in mgs of dry mycelium per flask			
	pH 4.0	pH 5.0	pH 6.0	pH 7.0
0.0	0.0	0.0	0.0	0.0
0.00625	8	..	..	..
0.0125	8	3	..	..
0.025	15	8	..	..
0.05	28	20	3	..
0.1	33	37	8	4
0.2	36	23	16	4
0.4	35	27	18	5
0.8	..	29	38	42
1.6	..	..	34	33
3.2	..	..	..	59

Table 1 gives the different treatments and the results. The foregoing picture remained essentially the same

<sup>1</sup> Published with the approval of the Director of the West Virginia Agricultural Experiment Station as Scientific Paper No. 314.

<sup>2</sup> F. C. Schmelkes, O. Wyss, H. C. Marks, B. J. Ludwig and F. B. Strandkov, *Proc. Soc. Exp. Biol. and Med.*, 50: 145, 1942.

<sup>3</sup> F. C. Schmelkes, *Jour. Bact.*, 45: 67, 1943.

<sup>4</sup> A. H. Brueckner, *Yale Jour. Bot. and Med.*, 15: 813, 1943.

when the agar medium of Tatum and Beadle<sup>5</sup> was used and the rate of growth was determined by measuring the diameter of the colonies. It should be stated that this fungus is variable, the amount of growth fluctuating over a wide range under apparently identical conditions. Nevertheless, the fundamental principle of its behavior remains the same, namely, that the effectiveness of *p*-aminobenzoic acid as a growth factor decreases with the increase in pH.

An opposite pH effect was observed by Stokes, Foster and Woodward<sup>6</sup> with a pyridoxin-requiring mutant of *Neurospora sitophila*. These investigators found that under certain conditions of nitrogen nutrition the fungus could synthesize pyridoxine at a rate necessary for normal growth if the pH remained above 6.2. However, in a medium containing no *p*-aminobenzoic acid the pH exerted no controlling effect on the *Neurospora crassa* mutant used in our work. In the presence of the vitamin the fungus attains maximum growth within a few days, whereas in its absence no growth will occur during that time. This failure to grow may continue for two or three weeks, but eventually, and then within only a few days, a rich growth will ensue regardless of the pH value. From the weight of the mycelium produced in such cultures, as well as from microbiological assay of the culture filtrate, it is evident that through some adaptive process the organism develops a latent ability to synthesize *p*-aminobenzoic acid during the prolonged incubation period. The fact that this synthesis and the growth resulting from it are not fundamentally influenced by the pH of the culture medium indicates that the pH effects observed in the early growth must be ascribed to changes in the effectiveness of the *p*-aminobenzoic acid.

Since *p*-aminobenzoic acid has a dissociation constant of about  $2 \times 10^{-5}$ , at pH 4.8 it exists in solution as equal amounts of molecules and ions. At pH 5.8 the molecular form decreases from 50 to 10 per cent. and above that value the portion present as the molecule drops almost tenfold with each unit rise in pH. Therefore, the efficiency of the vitamin in the nutrition of this organism appears to be a function of the molecular form rather than of the ion.

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<sup>5</sup> E. L. Tatum and G. W. Beadle, *Proc. Nat. Acad. Sci.*, 28: 234, 1942.

<sup>6</sup> J. L. Stokes, J. W. Foster and C. R. Woodward, Jr., *Arch. Biochem.*, 2: 235, 1943.

# RAPID AND STERILIZING EFFECT OF PENICILLIN SODIUM IN EXPERIMENTAL RELAPSING FEVER INFECTIONS AND ITS INEFFECTIVENESS IN THE TREATMENT OF TRYPANOSOMIASIS (TRYPANOSOMA LEWISI) AND TOXOPLASMOSIS<sup>1, 2</sup>

THE following preliminary report deals with the results obtained with penicillin sodium therapy in the following experimental infections: (1) trypanosomiasis, *T. lewisi*, in laboratory rats of a Wistar strain believed to be free from *Haemobartonella muris*; (2) toxoplasmosis, and (3) relapsing fever in Swiss mice. The penicillin sodium used in these experiments was kindly furnished by Dr. Chester Keefer.

(1) *Trypanosomiasis*. Six rats weighing about 70 grams each were used in testing the therapeutic value of penicillin sodium in trypanosomiasis. Treatment was started on 4 of the rats 6 days after their inoculation with a dilute suspension of blood containing adult trypanosomes. The infections in the 2 untreated rats served as controls. The routine therapy covered a period of 48 hours and consisted of the subcutaneous injection of 2,000 Oxford units of penicillin sodium dissolved in 1 cc distilled water every 3 hours, night and day, for 2 rats, and intraperitoneal injections of the drug in a similar manner for the other 2 rats. The total dose received by each of the 4 rats was 32,000 units, or 429,000 units per kilogram. Parasite counts were made 24 hours after the initial dose and daily thereafter for 5 days. No significant difference was noted between the counts for the treated and untreated animals. All infections ran a typical course. The trypanosomes in the blood of the treated animals appeared active, unharmed, and infected other rats, producing again typical infections.

(2) *Toxoplasmosis*. In the toxoplasma experiments the mice were infected by the intraperitoneal inoculation of large doses of a strain of *Toxoplasma* highly pathogenic for mice. Sixteen mice were infected.

Treatment of lot I, consisting of 4 mice, was started the 5th day after infection; each received 9,000 units, 500 units intraperitoneally in 0.5 cc saline every 3 hours. The treatment of lot II, also consisting of 4 mice, was started on the 9th day after infection. Each mouse received 500 units intraperitoneally in 0.5 cc saline to make a total dosage ranging from 6,500 to

<sup>1</sup> From the Department of Comparative Pathology and Tropical Medicine, Schools of Medicine and Public Health, Harvard University.

<sup>2</sup> A preliminary report.